CCGTTGGCCGAGAAGGAGGAGGGGCCGTGTCGGCGTCCAGCCCCTCGCGCCCAGGATGGACGTGCCAGCC AGGGTGTCCAGACGAGCGGCGGCGGCGGCGGCCAGGATGCTTCTGCGTACTGCCCGCGTCCCTCGCGAGTG CTGGTTCCTGCCGACCGCGCTGCTCTGCGCCTACGGCTTCTTCGCAAACCTCCGGCCGTCGGAGCCGTTCC TCACGCCCTACCTTCTGGGACCCGACAAGAACTTGACCGAGAGACAGGTCTACAATGAAATTTATCCGGTG TGGACGTACTCTTACCTGCTGCTGCTGTTTCCCGTGTTCCTTGCCACAGACTACCTCCGGTACAAGCCTGT CATCCTGCTGCAGGGACTCAGCCTGATTGTGACGTGGTTCATGCTGCTCTATGCCCAGGGACTGCTGGCCA TTCAGTTCTTGGAATTCTTCTACGGCATCGCCACAGCCACCGAAATCGCCTACTACTCCTATATCTATACT GTGGTGGACCTGGGCATGTACCAGAAAGTCACAAGCTACTGTAGAAGTGCCACCTTGGTGGGCTTTACAGT GGGCTCCGTCCTAGGGCAGATCCTCGTCTCCGTGGTGGGCTGGTCACTGTTCAGCTTGAACGTCATCTCCC TCACCTGTGTTTCTGTGGCTTTTGCTGTGGCCTGGTTTCTGCCTATGCCACAGAAGAGCCTCTTCTTTCAC CACATTCCTTCCTCTGTCATGGAGTGAACGGCCTCAAGGTACAAAACGGTGGCATCGTTACTGATACCCC AGCAGCTAACCATCTTCCTGGATGGGAGGACATTGAGTCAAAAATCCCTCTAAATTTAGATGAGCCTCCGG TGGAAGAACCGGAGGAGCCAAGCCAGACCGGCTGCGGGTGTTCAGAGTCCTGTGGAATGACTTCCTGATG TGTTATTCCTCCGCCCTCTGCTGTGGTCCGTGTGGTGGGCCCTGTCCACCTGCGGCTATTTCCAAGT GGTGAACTACGCGCAGGGATTGTGGGAGAAGGTGATGCCTTCTCAGAATGCTGACATCTACAATGGCGGTG TGGAGGCCGTTTCAACCTTGCTGGGTGCTAGTGCTGTTTTGCAGTTGGCTATATAAAGCTATCTTGGTCA ACTTGGGGAGAAATGACGTTGTTCCTGTGTTCTCCTGATTGCTGCTGCAGTGTATGTCATGGACACTGT GCAGAGCATCTGGGTGTGCTATGCATCCTATGTTGTCTTCAGAATCATCTACATGGTACTCATCACCATAG CAACTTTCCAGATTGCTGCGAACCTCAGCATGGAACGTTACGCCCTTGTGTTCGGCGTGAACACCTTCATT GCCCTGGCATTGCAGACTCTGCTCAGTTGTCGTGGATGCCAGGGGCCTTGGCTTATGTATCACCAC TCAGTTCCTGATTTACGCCAGTTACTTCGCAGCCATCTCTGTGGTTTTCCTGGCGAATGGCATAGTCAGTA TTATAAAGAAATGCAGAAAGCAGGAAGATCCCAGCTCCAGCCCCCAAGCCTCCACGTCCTAACGGGCTCCC GAAGTGCTGCTTCCAAGCAAGGATTTTGCACCGCAGCTGCTTGGATGTATTTAAACTCCTCATGGTTC AGATAGCTATTTCTGAATGTATATTTCATGGCTTCAAAGCAGCTACTCAACTAACACCTTGCAGTCTTGGA AAACCCACAAAACTTGATTGTGAAAAACCGAATAACCAAGCGCGTCTGCTCTTTCCCTGATTCGCATG TGACTGTGATGCTTTCCAGTCACATTCATCACGCACTCAGACCTGTGGCCTGGTGGGACCAGGGCTTCAGG AGCCACAGGATGGTACAAGCCTCGACAGACACGTTCTGTCAGCACTTGCCCCGGCCACCTCATTCTGGTTT CAGTGTTACTTGTGCGCATGTGTGTGTGTCTGCAGATGGAAATCATTCCCCACTGGCAGTATCTGCTCG GGTTCAACGCTCTGTCCTCTGAGGAGTGTTGTGTCTGATTTTATTTTAAAAGTTCACGGTATGAGAGTTAG TGCTTCTTCCCAATTTGACCGTTGTATATTTTTGGAAACGTTCTTTAGAATACATTTCTGCATTATTTGTA TGCTTCCCAGAGAAGCTCATTTCATTACAAAAGGCACATTTTAAAGCCTGCTGATAACTGAGGAGGGCTAA TGAGATAGGTTTGCTCGTCTGTAATAGTTATGTATGAAGGACTCTTAATTGCAACTGAAAAGGTCGTGTAT AGGTTAGAGATACAGGGAGCCCATTTTATATTTTGCATACCCTTTTATTTTCCAAAACAAAATGAGCTCTTTT CCCTTGAGACAATATCATTCCCATATACCTCTCATTGTCTTGGCTTTCTTATCCAAGACGAGAAGATATCA GTCGGAACTGGATTATTCCACAGCCTTTTTATAAACTGAGCCTCTTCTTAATGATTGTTCTGGGCTTGGCA GTAGGATAGACTTGATGCCTGCGTTTTGGACCTTAGACCTGCCCGCCTTCGTTCCTACAGTTAGATCATCT TGAGAGATACTTAAAAGTATCTCCTCCTTACTTGAAAGAATGATGTTCTACATGCTAATATTTGTGAGACA TGTTGACCTTGTTAAGACGGACGTAGCTGCACGGTATTCTCAATACTGAGATTGCAAAACTGAAGCTTGAC AAGTGTGTGGAAGACCCTGGCTCAAGTTCCAGCACTGGAAAGACCAAAGTGCAAACGTGCATGGGAGGAGT GAGGGTAACAGAGGCCATGGCGTACGTCTTCCTTTGCAGCTAGGGAAAGAGAAGAACACTAAGGAGATGGA GAACTAAGGTCAGAGTAGCAGTCTCCAGTCTTACATTTTGGTCTCTTTCCTCCTATACTTCCTTGTTGCTC AATAACATGTATTATGGCACAATCAAATTGTTCACATTACCAAAGCAATATTTCTTTGGGATTCAGTTCAG TGTTTGTGGCATCTAATCTGATCCTTCTTTACGTGTCTAAATCAAGACTGTATCCACATTTTACCACGCGG CCATACTTGCAGAATGCAGACCCTAGTGGGCTGTACTGTATGCACTTTGATGAAGACGTGAAAAGAATCTG CTGTACTTTTTATTCAATCTGTATAGACTATAAAACTATTTTTATTAAATAATATTTTACAGTAAAAAAA (SEO ID NO:1)

MDVPARVSRRAAAAAARMLLRTARVPRECWFLPTALLCAYGFFANLRPSEPFLTPYLLG
PDKNLTERQVYNEIYPVWTYSYLLLLFPVFLATDYLRYKPVILLQGLSLIVTWFMLLYA
QGLLAIQFLEFFYGIATATEIAYYSYIYTVVDLGMYQKVTSYCRSATLVGFTVGSVLGQ
ILVSVVGWSLFSLNVISLTCVSVAFAVAWFLPMPQKSLFFHHIPSSCHGVNGLKVQNGG
IVTDTPAANHLPGWEDIESKIPLNLDEPPVEEPEEPKPDRLRVFRVLWNDFLMCYSSRP
LLCWSVWWALSTCGYFQVVNYAQGLWEKVMPSQNADIYNGGVEAVSTLLGASAVFAVGY
IKLSWSTWGEMTLFLCSLLIAAAVYVMDTVQSIWVCYASYVVFRIIYMVLITIATFQIA
ANLSMERYALVFGVNTFIALALQTLLTLIVVDARGLGLCITTQFLIYASYFAAISVVFL
ANGIVSIIKKCRKQEDPSSSPQASTS (SEQ ID NO: 2)

FIGURE 2

Sequenc Length: 3554 bp

S quence Del t d: from base 484 to base 526

b Id underlined t xt = deleted in gene sequence

plain text = gene sequence flanking deleted sequence

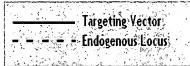
GGCGGACTTAGGGAAAGGGCGTTCGGCTAGCGAGCTGTGGCCGCCGGCGGCGGTGGGGACTCCAAGCACCTTGACCCTG GAGGGGCCGTGTCGGCGTCCAGCCCCTCGCGCCCAGGATGGACGTGCCAGGCTGTCCAGACGAGCGGCGGCGGCG GCGGCCAGGATGCTTCTGCGTACTGCCCGCGTCCCTCGCGAGTGCTGGTTCCTGCCGACCGCGCTGCTCTGCGCCTACGG CTTCTTCGCAAACCTCCGGCCGTCGGAGCCGTTCCTCACGCCCTACCTTCTGGGACCCGACAAGAACTTGACCGAGAGAC ${\tt AGGTCTACAATGAAATTTATCCGGTGTGGACGTACTCTTACCTGCTGCTGCTGTTTCCCGTGTTTCCTTGCCACAGACTAC}$ $\texttt{CTC} \underline{\textbf{CGGTACAAGCCTGTCATCCTGCAGGGACTCAGCCTGATTG}} \texttt{TGACGTGGTTCATGCTGCTCTATGCCCAGGGACT}$ GCTGGCCATTCAGTTCTTGGAATTCTTCTACGGCATCGCCACAGCCACCGAAATCGCCTACTACTCCTATATCTATACTG TGGTGGACCTGGGCATGTACCAGAAAGTCACAAGCTACTGTAGAAGTGCCACCTTGGTGGGCTTTACAGTGGGCTCCGTC $\tt CTAGGGCAGATCCTCGTGTGGGGGGGGGTGGTCACTGTTCAGCTTGAACGTCATCTCCCTCACCTGTGTTTCTGTGGC$ ACGGCCTCAAGGTACAAAACGGTGGCATCGTTACTGATACCCCAGCAGCTAACCATCTTCCTGGATGGGAGGACATTGAG TCAAAAATCCCTCTAAATTTAGATGAGCCTCCGGTGGAAGAACCGGAGGAGCCCAAGCCAGACCGGCTGCGGGTGTTCAG AGTCCTGTGGAATGACTTCCTGATGTGTTATTCCTCCCGCCCTCTGCTCTGCTGGTCCGTGTGGGGCCCTGTCCACCT GCGGCTATTTCCAAGTGGTGAACTACGCGCAGGGATTGTGGGAGAAGGTGATGCCTTCTCAGAATGCTGACATCTACAAT GGCGGTGTGGAGGCCGTTTCAACCTTGCTGGGTGCTAGTGCTGTGTTTGCAGTTGGCTATATAAAGCTATCTTGGTCAAC TTGGGGAGAAATGACGTTGTTCCTGTGTTCTCCTGATTGCTGCTGCAGTGTATGTCATGGACACTGTGCAGAGCATCT GGGTGTGCTATGCATCCTATGTTGTCTTCAGAATCATCTACATGGTACTCATCACCATAGCAACTTTCCAGATTGCTGCG AACCTCAGCATGGAACGTTACGCCCTTGTGTTCGGCGTGAACACCTTCATTGCCCTGGCATTGCAGACTCTGCTCACTCT ${\tt GATTGTCGTGGATGCCAGGGGCCTTGGCTTATGTATCACCACTCAGTTCCTGATTTACGCCAGTTACTTCGCAGCCATCT}$ CTGTGGTTTTCCTGGCGAATGGCATAGTCAGTATTATAAAGAAATGCAGAAAGCAGGAAGATCCCAGCTCCAGCCCCCAA AACTCCTCATGGTTCAGATAGCTATTTCTGAATGTATATTTCATGGCTTCAAAGCAGCTACTCAACTAACACCTTGCAGT CCCACAAAACTTGATTGTGAAAAACCGAATAACCAAGCAGCGCGTCTGCTCTTTCCCTGATTCGCATGTGACTGTGATGC TTTCCAGTCACATTCATCACGCACTCAGACCTGTGGCCTGGTGGGACCAGGGCTTCAGGAGCCACAGGATGGTACAAGCC TCTGCAGATGGAAATCATTCCCCACTGGCAGTATCTGCTCGGGTTCAACGCTCTGTCCTCTGAGGAGTGTTGTGTCTGAT TTTATTTTAAAAGTTCACGGTATGAGAGTTAGTGCTTCTTCCCAATTTGACCGTTGTATATTTTTGGAAACGTTCTTTAGAATACATTTCTGCATTATTTGTATGCTTCCCAGAGAAGCTCATTTCATTACAAAAGGCACATTTTAAAGCCTGCTGATAA TGTATAGGTTAGAGATACAGGGAGCCCATTTTATATTTGCATACCCTTTTATTTCCAAAACAAAATGAGCTCTTTTCCCT ${\tt TGAGACAATATCATTCCCATATACCTCTCATTGTCTTGGCTTTCTTATCCAAGACGAGAAGATATCAGTCGGAACTGGAT}$ TATTCCACAGCCTTTTTATAAACTGAGCCTCTTCTTAATGATTGTTCTGGGGCTTGGCAGTAGGATAGACTTGATGCCTGC GTTTTGGACCTTAGACCTGCCCGCCTTCGTTCCTACAGTTAGATCATCTTGAGAGATACTTAAAAGTATCTCCTCCTTAC TTGAAAGAATGATGTTCTACATGCTAATATTTGTGAGACATGAAAACTATTTCAAAGCCAACTTTGTTGTCTTGTTGTAT GATTGCAAAACTGAAGCTTGACAAGTGTGTGGAAGACCCTGGCTCAAGTTCCAGCACTGGAAAGACCAAAGTGCAAACGT GCATGGGAGGGTGAGGGTAACAGAGGCCATGGCGTACGTCTTCCTTTGCAGCTAGGGAAAGAGAAGAACACTAAGGAGA TGGAGAACTAAGGTCAGAGTAGCAGTCTCCAGTCTTACATTTTGGTCTCTTTCCTCCTATACTTCCTTGTTGCTCTATAA ${\tt TGGCACAATCAAATTGTTCACATTACCAAAGCAATATTTCTTTGGGATTCAGTTCAGTGTTTGTGGCATCTAATCTGATC}$ $\tt CTTCTTTACGTGTCTAAATCAAGACTGTATCCACATTTTACCACGCGGCCATACTTGCAGAATGCAGACCCTAGTGGGCT$ GTACTGTATGCACTTTGATGAAGACGTGAAAAGAATCTGCTGTACTTTTTATTCAATCTGTATAGACTATAAAACTATTT TTATTAAATAAATATTTTACAGTAAAAAAAAAA (SEO ID NO:1)

FIGURE 3

Targeting Vector* (genomic sequence)

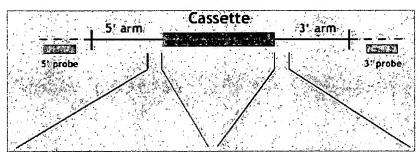
Arm Length: 5': 4.5 kb

3': 0.6 kb



Not drawn to scale

LacZ-Neo



AGGTCTACAATGAAATTTATCCGG TGTGGACGTACTCTTACCTGCTGC TGCTGTTTCCCGTGTTCCTTGCCA CAGACTACCTC<3' (SEQ ID NO:3)

>TTACTGTGGCCAGTATTTCTC 5'>TGACGTGGTTCATGCTGCTCT CGGGGATAAGGGAGTGTTGGTGGG ATGCCCAGGGACTGCTGGCCATTC CTGTTTTGTAGGAATACATTCTTA AGTTCTTGGAATTCTTCTACGGCA TGGCTTGTCGGGTCTGTTGATCAC TCGCCACAGCCACCGAAATCGCCT TAACGAGCTTTCACTCTTCCTACC ACTACTCCTATATCTATACTGTGG TGGACCTGGGCATGTACCAGAAAG TCACAAGCTACTGTAGAAGTGCCA CCTTGGTGGGCTTTACAGTGGGCT CCGTCCTAGGG<3' (SEQ ID NO:4)

FIGURE 4

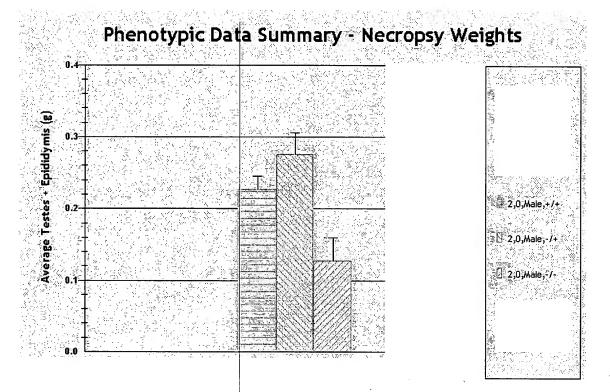


FIGURE 5

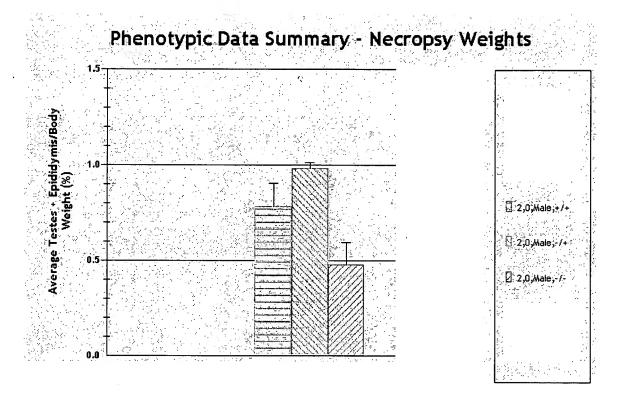


FIGURE 6